

INTERNATIONAL SEARCH REPORT

Intern application No

PCT/US 01/26566

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K14/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

SEQUENCE SEARCH

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99 14336 A (PROMEGA CORPORATION (US); WOOD KEITH V.; HALL MARY P.) 25 March 1999 (1999-03-25) cited in the application	47
Y	abstract	46
A	page 89 -page 90; claim 16 page 104; claims 21,22; figure 106 figure 46	18,19
Y	WOOD K.V.: "The chemical mechanism and evolutionary development of beetle bioluminescence" PHOTOCHEMISTRY AND PHOTOBIOLOGY, vol. 62, no. 4, 1995, pages 662-673, XP000983576 ISSN: 0031-8655 page 669, left-hand column	46
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Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

° Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *G* document member of the same patent family

Date of the actual completion of the international search

13 February 2003

Date of mailing of the international search report

28/02/2003

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 95 18853 A (PROMEGA CORPORATION (US); WOOD KEITH V.; HALL MARY P.) 13 July 1995 (1995-07-13) cited in the application	47
A	page 19 -page 21 ----	18, 19
X	DATABASE EBI 'Online! 8 August 2000 (2000-08-08) FERBITZ L. ET AL.: "A synthetic gene coding for Renilla luciferase is a versatile expression marker in green algae" Database accession no. AY004213 XP002230923	47
A	the whole document ----	17
X	US 5 670 356 A (PROMEGA CORPORATION (US); SHERF BRUCE A.; WOOD KEITH V.) 23 September 1997 (1997-09-23) cited in the application the whole document ----	48-53, 55-59, 65,66
X	PAN W. ET AL.: "Vaccine candidate MSP-1 from Plasmodium falciparum: a redesigned 4917 bp polynucleotide enables synthesis and isolation of full-length protein from Escherichia coli and mammalian cells" NUCLEIC ACIDS RESEARCH, vol. 27, no. 4, 15 February 1999 (1999-02-15), pages 1094-1103, XP000953100 ISSN: 0305-1048 page 1095, left-hand column page 1096, right-hand column -page 1097 ----	48,49, 52,53, 55-58, 65,66
X	KIM C.H. ET AL.: "Codon optimization for high-level expression of human erythropoietin (EPO) in mammalian cells" GENE, vol. 199, no. 1-2, 15 October 1997 (1997-10-15), pages 293-301, XP004126394 ISSN: 0378-1119 the whole document -----	55

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Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.: 1-16, 20-45, 54, 60-64 all in part
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☒ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 10, 17 all totally; 1-9, 14-16, 20-45, 47, 54, 60-64 all partially

A synthetic nucleic acid molecule encoding a Renilla luciferase and related products, as claimed in the claims indicated above.

2. Claims: 12, 18 all totally; 1-9, 11, 14-16, 20-47, 54, 60-64 all partially

A synthetic nucleic acid molecule encoding a beetle luciferase and related products, as claimed in the claims indicated above.

3. Claims: 13, 19 all totally; 1-9, 11, 14-16, 20-47, 54, 60-64 all partially

A synthetic nucleic acid molecule encoding a beetle luciferase and related products, as claimed in the claims indicated above.

4. Claims: 48-53, 55-59, 65, 66 all totally; 54 partially

Method(s) and related products, as claimed in the claims indicated above

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-16, 20-45, 54, 60-64 all in part

Present claims 1-16, 20-34 and 60-62 relate to an extremely large number of possible synthetic nucleic acid molecules without giving a true technical characterization of said molecules.

In fact, said molecules are defined by reference to the following parameter(s), desirable characteristics and/or properties: (1) comprising at least 300 nucleotides of a coding region for a polypeptide (inter alia reporter molecule, selectable marker protein, (Renilla, beetle) luciferase); (2) having a codon composition differing at more than 25% (or 35%, 45%, 55%) of the codons from a wild type nucleic acid sequence encoding a polypeptide; (3) having at least 3-fold (or 5-fold) fewer transcription regulatory sequences relative to the average number of such sequences resulting from random selections of codons at the codons which differ, (3.bis) wherein the transcription regulatory sequences are selected from the group consisting of transcription factor binding sequences, intron splice sites, poly (A) addition sites and promoter sequences; (4) wherein the polypeptide encoded by the synthetic nucleic acid molecule has at least 85% (or 90% contiguous, or 100%) sequence identity to the polypeptide encoded by the wild type nucleic acid sequence; (2bis) wherein the majority of codons which differ are the ones that are preferred codons of a desired host cell (inter alia mammals, humans, plants, see also claims 20-23 and 25-34); (5) wherein said synthetic nucleic acid molecule is expressed in a mammalian host cell at a level which is greater (or at least 110%) than that of the wild type nucleic acid sequence.

The claims cover all molecules having this parameters, characteristics or properties, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such molecules, i.e. the ones mentioned in claims 17-19.

In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible.

Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define a nucleic acid molecule by reference to parameters and to a result to be achieved. It is impossible to compare the parameters, and the desirable characteristics and properties the applicant has chosen to employ, with what is set out in the prior art.

Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible.

Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the nucleic acid molecules concerned in claims 17-19.

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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

The same remarks apply mutatis mutandis to claims 35-45, 54, 63 and 64.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

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Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9914336	A	25-03-1999	AU 754312 B2	14-11-2002
			AU 9492198 A	05-04-1999
			CA 2301828 A1	25-03-1999
			EP 1015601 A2	05-07-2000
			JP 2001516585 T	02-10-2001
			WO 9914336 A2	25-03-1999
WO 9518853	A	13-07-1995	AU 698424 B2	29-10-1998
			AU 1830395 A	01-08-1995
			CA 2157476 A1	13-07-1995
			EP 0689587 A1	03-01-1996
			JP 8510387 T	05-11-1996
			WO 9518853 A1	13-07-1995
			US 6387675 B1	14-05-2002
US 5670356	A	23-09-1997	NONE	